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APPLICATION NO.	FILED DATE	FIRST NAMED INVENTOR	ATTORNEY OR AGENT NO.	CONFIRMATION NO.
10/119,913	04/10/2002	Andrey J. Zarev	13071-007001	9399
22428 7590 01/11/2003 WOLF GREENFIELD & SACKS, PC FEDERAL RESERVE PLAZA 600 ATLANTIC AVENUE BOSTON, MA 02210-2211			EXAMINER RE-SNER, WILLIAM R	
			ART UNIT	PAPER NUMBER
			1741	
DATE MAILED FOR 01/11/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-SOC (Rev. 10/03)

## Office Action Summary

COMM 19,617

ZARUR ET AL

Examiner

Art Unit

William H. Seiner

1744

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(c).

## Status

- 1) ☒ Responsive to communication(s) filed on 8/6/04, 10/20/04, 11/8/04.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 2-7, 11-28, 32-38, 42-48 and 52-55 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-7, 11-28, 32-38, 42-48 and 52-55 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 April 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s), including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-802)
- 2) ☐ Notice of Draftsperson's Patent Examining Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No.(s)/Mailing Date 0/6, 10/20, 11/8

- 4) ☐ Interview Summary (PTO-413)  
Paper No.(s)/Mailing Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

U.S. Patent and Trademark Office

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Part of Paper No./Mailing Date 20050107

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### DETAILED ACTION

#### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 8/6/2004 and 10/20/2004 have been entered.

#### *Information Disclosure Statement*

2. The information disclosure statements filed 8/6/2004, 10/20/2004 and 11/8/2004 have been considered and made of record.

#### *Drawings*

3. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the claimed microfermentor device including a plurality of reaction chambers each with inlet and outlet ports and channels; the gas headspace with an inlet and outlet port; and an optical sensor must be shown on the feature(s) canceled from the claim(s). No new matter should be entered. Note the instant claims have been substantially amended in view of the originally filed claims and the drawings fail to reflect a device that includes at least these claimed features recited in all of the independent claims of record.

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Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement-drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

#### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2-7, 11-28, 32-38, 42-48, 52-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claims 5, 12, 13 and 15, the claims recite that the cell growth chambers are formed within the polymeric substrate and each includes an inlet port and an outlet port. The

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claims further recite that the substrate includes at least a first and second channel fabricated into the surface of the substrate and fluidly connected to the cell growth chamber. In view of the current claim language, it is not clear if the recited first and second channels are provided in fluid communication with the previously recited inlet and outlet port or are providing additional an additional inlet and outlet with respect to the cell growth chamber. Clarification and/or correction is requested. Claims 2-7, 11-19 26-28, 30-38, 42-48 and 52-55 are indefinite in view of their dependency on claims 5, 12, 13 or 15.

In claim 20, line 9, "the reaction system" lacks antecedent basis. It is not readily apparent in view of the previously recited claim language what previously recited structural element(s) are related to "the reaction system". Clarification and/or correction is requested. Claims 21-25 are indefinite in view of their dependency on claim 20.

### *Claim Rejections - 35 USC § 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (WO 99/55827) in view of Cremonese (US 4,839,292).

The reference of Thomas discloses a method of screening a plurality of test compounds that includes providing a polymeric substrate (See page 7, lines 8-26) having a surface into which a plurality of reaction chambers (6) are constructed to operate in parallel (See Figure 1/3). Each reaction chamber (6) includes a cell growth chamber (2) containing cells and is fluidly connected to an inlet channel (1) and an outlet channel (4). Each of the growth chambers is associated with a gas permeable membrane that is water vapor impermeable (See page 6, line 24, to page 7, line 6). The method includes introducing one or more test substances to the cells in the growth chambers and monitoring the effect of the test substances on the cells by means of optical detection within the cell growth chamber (See page 3, lines 7-24 and page 14, lines 9-11). As shown in Example 1, the volume of the growth chamber is less than 1  $\mu$ l (See page 18, lines 4-

6)

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With respect to claim 20, while the reference discloses the use of a gas permeable membrane as discussed above and incubation of the device in a tissue culture incubator (See page 19, lines 6-8), the reference does not specifically disclose that the gas permeable membrane is provided with a gas headspace with an inlet port and outlet port on the side opposite to the cell growth chamber.

The reference of Cremonese discloses that it is known in the art to provide gas to a non-culture side of a gas permeable membrane (20) by providing a gas headspace (6) including a gas inlet port (16) and a gas outlet port (18).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ a gas headspace creating device as disclosed by the reference of Cremonese with the gas permeable membrane of the primary reference of Thomas for the known and expected result of providing an art recognized means for controlling the gas concentration and incubation conditions with respect to a culture chamber provided on the opposite side of a gas permeable membrane. Note the instant claims do not preclude the use of a single gas headspace in communication and/or single gas permeable membrane that is common to all of the cell growth chambers.

With respect to the types of cells employed and/or biological responses detected of claims 21-25, the reference of Thomas discloses a number of types of responses and cell types that can be used (See page 10, line 13, to page 11, line 8).

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10. Claims 2-11, 14 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (WO 99/55827) in view of Cremonese (US 4,839,792) taken further in view of Sheppard et al. (US 6,143,247) or Mian et al. (US 6,319,469).

The combination of the references of Thomas and Cremonese has been discussed above.

Claims 5-7 differ by reciting that the device includes a mixing chamber in fluid communication with the inlet channel to the cell growth chamber.

The reference of Sheppard, Jr. et al. discloses a microchamber test device that includes plural chambers and discusses mixing in the device (See Figures 3C-3F and column 26, lines 31-46).

The reference of Mian et al. discloses a microchamber test device that includes plural chambers and discusses mixing in the device (See column 7, line 4).

In view of these teachings, it would have been obvious to one of ordinary skill in the art to provide the device of the primary reference with mixing chambers for the known and expected result of mixing any added reagents in the culture medium prior to contacting the cells in the chamber so as to ensure a uniform concentration of reagent in the culture chamber.

With respect to claims 2-4, the volume of the growth chamber is less than 1  $\mu$ l (See page 18, lines 4-6, of Thomas)

With respect to claim 11, both the references of Sheppard et al. and Mian et al. disclose that the use of temperature control elements, i.e. heaters and temperature sensors, as known in microfluidic devices for the known and expected result of maintaining the chambers at a desired temperature (See column 25, lines 37-67, of Sheppard et al. and column 15, line 65, to column 16, line 17, of Mian et al.).



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With respect to claim 14, the optical components disclosed by the reference of Thomas would be capable of detecting optical density within the cell growth chamber.

With respect to claims 16-19, the reference of Thomas discloses a device that includes more than 20 cell growth chambers (See Figure 1). With respect to the use of additional chambers over the number of 50 or 100, mere duplication of parts has no patentable significance unless a new and unexpected result is produced (In re Harza, 274 F.2d 669, 124 USPQ 378 (CCPA 1960)).

11. Claims 12, 13, 15, 26-28, 32-38, 42-48 and 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (WO 99/55827) in view of Cremonese (US 4,839,292) taken further in view of Kroy et al. (US 5,252,294).

The combination of the references of Thomas and Cremonese has been discussed above.

The claims differ by reciting that the chamber includes sensors for monitoring a number of different parameters within the chamber. Specifically claim 12 recites "a sensor for monitoring pH within the chamber", claim 13 recites "a sensor for monitoring the pressure within the chamber" and claim 15 recites a sensor for monitoring glucose concentration within the chamber.

The reference of Kroy et al. discloses that it is known in the art to provide a microfluidic chamber with a number of sensors to detect different parameters within the detection chamber (See the entire document). With respect to pH monitoring see column 4, lines 25-26 and line 39. With respect to pressure sensing, see column 4, line 15, and column 5, line 38. With respect to glucose sensing, see column 4, line 39.

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In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the device of the primary reference with a number of parameter sensors so as to monitor the culture conditions which is conventional in the culture art.

With respect to claims 26-28, 36-38 and 46-48, the volume of the growth chamber is less than 1 µl (See page 18, lines 4-6, of Thomas).

With respect to claims 32-35, 42-45 and 52-55, the reference of Thomas discloses a device that includes more than 20 cell growth chambers (See Figure 1). With respect to the use of additional chambers over the number of 50 or 100, mere duplication of parts has no patentable significance unless a new and unexpected result is produced (In re. Harza, 274 F.2d 669, 124 USPQ 378 (CCPA 1960)).

12. Claims 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (WO 99/55827) in view of Freeman (US 6,653,124).

The reference of Thomas discloses a method of screening a plurality of test compounds that includes providing a polymeric substrate (See page 7, lines 8-26) having a surface into which a plurality of reaction chambers (6) are constructed to operate in parallel (See Figure 1/3). Each reaction chamber (6) includes a cell growth chamber (2) containing cells and is fluidly connected to an inlet channel (1) and an outlet channel (4). Each of the growth chambers is associated with a gas permeable membrane that is water vapor impermeable (See page 6, line 24, to page 7, line 6). The method includes introducing one or more test substances to the cells in the growth chambers and monitoring the effect of the test substances on the cells by means of optical detection within the cell growth chamber (See page 3, lines 7-24 and page 14, lines 9-11).

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As shown in Example 1, the volume of the growth chamber is less than 1 $\mu$ l (See page 18, lines 4-

6)

With respect to claim 20, while the reference discloses the use of a gas permeable membrane as discussed above and incubation of the device in a tissue culture incubator (See page 19, lines 6-8), the reference does not specifically disclose that the gas permeable membrane is provided with a gas headspace with an inlet port and outlet port on the side opposite to the cell growth chamber.

The reference of Freeman discloses that it is known in the art to separate a cell growth chamber (12) from a chamber (44) by a membrane wherein the membrane separates the cell growth chamber (12) from a chamber (44) that can provide nutrient exchange including gas exchange (See column 24, line 56, to column 25, line 2). The reference discloses that the chambers (44) can be common to all the cell growth chambers (12) or alternatively include specialized conduits to individually connect to each chamber (12).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ a gas headspace creating device as disclosed by the reference of Freeman with the gas permeable membrane of the primary reference of Thomas for the known and expected result of providing an art recognized means for controlling the gas concentration and incubation conditions with respect to a culture chamber provided on the opposite side of a gas permeable membrane. Note the reference of Freeman suggests a headspace that is common to all the chambers or the use of conduits that individually connect to each growth chamber.

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With respect to the types of cells employed and/or biological responses detected of claims 21-25, the reference of Thomas discloses a number of types of responses and cell types that can be used (See page 10, line 13, to page 11, line 8).

13. Claims 2-11, 14 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (WO 99/55827) in view of Freeman (US 6,653,124) taken further in view of Sheppard et al. (US 6,143,247) or Mian et al. (US 6,319,469).

The combination of the references of Thomas and Freeman has been discussed above.

Claims 5-7 differ by reciting that the device includes a mixing chamber in fluid communication with the inlet channel to the cell growth chamber.

The reference of Sheppard, Jr. et al. discloses a microchamber test device that includes plural chambers and discusses mixing in the device (See Figures 3C-3F and column 26, lines 31-46).

The reference of Mian et al. discloses a microchamber test device that includes plural chambers and discusses mixing in the device (See column 7, line 4).

In view of these teachings, it would have been obvious to one of ordinary skill in the art to provide the device of the primary reference with mixing chambers for the known and expected result of mixing any added reagents in the culture medium prior to contacting the cells in the chamber so as to ensure a uniform concentration of reagent in the culture chamber.

With respect to claims 2-4, the volume of the growth chamber is less than 1  $\mu$ l (See page 18, lines 4-6, of Thomas)

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With respect to claim 11, both the references of Sheppard et al. and Mian et al. disclose that the use of temperature control elements, i.e. heaters and temperature sensors, as known in microfluidic devices for the known and expected result of maintaining the chambers at a desired temperature (See column 25, lines 37-67, of Sheppard et al. and column 15, line 65, to column 16, line 17, of Mian et al.).

With respect to claim 14, the optical components disclosed by the reference of Thomas would be capable of detecting optical density within the cell growth chamber.

With respect to claims 16-19, the reference of Thomas discloses a device that includes more than 20 cell growth chambers (See Figure 1). With respect to the use of additional chambers over the number of 50 or 100, mere duplication of parts has no patentable significance unless a new and unexpected result is produced (In re Harza, 274 F.2d 669, 124 USPQ 378 (CCPA 1960)).

14. Claims 12, 13, 15, 26-28, 32-38, 42-48 and 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (WO 99/55827) in view of Freeman (US 6,653,124) taken further in view of Kroy et al. (US 5,252,294).

The combination of the references of Thomas and Freeman has been discussed above.

The claims differ by reciting that the chamber includes sensors for monitoring a number of different parameters within the chamber. Specifically claim 12 recites "a sensor for monitoring pH within the chamber", claim 13 recites "a sensor for monitoring the pressure within the chamber" and claim 15 recites a sensor for monitoring glucose concentration within the chamber.

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The reference of Kroy et al. discloses that it is known in the art to provide a microfluidic chamber with a number of sensors to detect different parameters within the detection chamber (See the entire document). With respect to pH monitoring see column 4, lines 25-26 and line 39. With respect to pressure sensing, see column 4, line 15, and column 5, line 38. With respect to glucose sensing, see column 4, line 39.

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the device of the primary reference with a number of parameter sensors so as to monitor the culture conditions which is conventional in the culture art.

With respect to claims 26-28, 36-38 and 46-48, the volume of the growth chamber is less than 1 µl (See page 18, lines 4-6, of Thomas).

With respect to claims 32-35, 42-45 and 52-55, the reference of Thomas discloses a device that includes more than 20 cell growth chambers (See Figure 1). With respect to the use of additional chambers over the number of 50 or 100, mere duplication of parts has no patentable significance unless a new and unexpected result is produced (In re Harza, 274 F.2d 669, 124 USPQ 378 (CCPA 1960)).

15. Claims 2-7, 11-28, 32-38, 42-48 and 52-55 are rejected under 35 U.S.C. 103(a) as being obvious over Zarur et al. (Jury et al. US 2004/0121454 or WO 01/68257) in view of Thomas (WO 99/55827) and Freeman (US 6,653,124).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37

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CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(I)(1) and § 706.02(I)(2).

The reference of Zarur et al. discloses a microfermentor device (10) manufactured from a plastic substrate (See paragraph [0034]) that can include a plurality of reaction or cell growth chambers (16) that can operate in parallel (See paragraph [0027]). As shown in Figure 1, the cell growth chamber (16) includes inlet and outlet ports and channels. The reference discloses that the reaction chamber (16) is less than 1000 microliters (See paragraphs [0041] and [0035]) and the reference discloses the use of a mixing chamber (12).

While the reference of Zarur et al. discloses the use of membranes for the separation of products and/or metabolites from the cells (See paragraphs [0046] and [0047]), claims 5, 12, 13 and 15 differ by reciting that the device includes a gas permeable membrane and a gas headspace with fluid inlet and outlet.

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The reference of Thomas discloses that it is conventional in the art to provide a cell culture chamber of a microfluidic device with a gas permeable membrane (See page 6, line 24, to page 7, line 6) so as to provide the cells with oxygen for metabolism.

The reference of Freeman discloses that it is conventional in the art to employ a membrane (40) and headspace (44) for exchanging nutrients with a cell growth chamber in a microfluidic device.

In view of these teachings, it would have been obvious to one of ordinary skill in the art to provide a gas permeable membrane in communication with growth chamber (16) as suggested by the reference of Thomas for the known and expected result of providing an art recognized means for providing oxygen to the cell growth chamber. The use of a headspace as suggested by Freeman and Zarur et al. would have been obvious for the known and expected result of providing an art recognized means for individually addressing each growth chamber with a specific culture gas concentration.

With respect to claims 2-4, 26-28, 36-38 and 46-48, the reference of Zarur et al. discloses that the reaction chamber (16) is less than 1 microliters (See paragraphs [0041] and [0035]).

With respect to claims 16-19, 33-35, 42-45 and 52-55, the reference of Zarur et al. discloses that more than 100 growth chambers can be provided (See paragraph [0051]).

With respect to the use of an optical sensor of claims 5, 12, 13-15 and 20, the reference of Thomas et al. discloses that it is known in the art to provide an optical sensor and optically interrogate the cell growth chamber of a microfluidic culture device (See page 14, lines 9-11).



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In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the system of the primary reference with an optical sensor for the known and expected result of monitoring the cell growth in the cell growth chamber.

With respect to the sensors of claims 11, 12, 13 and 15, the reference of Zarur et al. discloses the use of all of these sensor devices (See paragraphs [0030] and [0049]).

With respect to the method of testing compounds of claims 20-25, the reference of Thomas discloses a method of screening a plurality of test compounds that includes providing a polymeric substrate (See page 7, lines 8-26) having a surface into which a plurality of reaction chambers (6) are constructed to operate in parallel (See Figure 1/3). Each reaction chamber (6) includes a cell growth chamber (2) containing cells and is fluidly connected to an inlet channel (1) and an outlet channel (4). Each of the growth chambers is associated with a gas permeable membrane that is water vapor impermeable (See page 6, line 24, to page 7, line 6). The method includes introducing one or more test substances to the cells in the growth chambers and monitoring the effect of the test substances on the cells by means of optical detection within the cell growth chamber (See page 3, lines 7-24 and page 14, lines 9-11).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ the device of the primary reference for the monitoring the response of cell to test compounds as suggested by the reference of Thomas for the known and expected result of providing an alternative device recognized in the art for culturing cells and determining their response to test compounds.

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With respect to the types of cells employed and/or biological responses detected of claims 21-25, the reference of Thomas discloses a number of types of responses and cell types that can be used (See page 10, line 13, to page 11, line 8).

### *Double Patenting*

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 2-7, 11-19, 26-29, 32-38, 42-48 and 52-55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 156-173 of copending Application No. 09/707,852 in view of Thomas (WO 99/55827).

Claims 156-173 of application 09/707,852 encompass a microfermentor device that is substantially the same as that instantly claimed. The claim encompass a plastic substrate that includes a plurality of cell culture chambers formed therein wherein the volume of the chambers is less than 1000 microliters and the chambers includes a fluid inlet and outlet. The device also includes a gas permeable membrane and gas enclosure with an inlet and outlet.

The instant claims differ by reciting that the device includes an optical sensor.

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The reference of Thomas discloses that it is known in the art to provide an optical sensor and optically interrogate the cell growth chamber of a microfluidic culture device (See page 14, lines 9-11).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the system of the primary reference with an optical sensor for the known and expected result of monitoring the cell growth in the cell growth chamber.

This is a provisional obviousness-type double patenting rejection

18. Claims 2-7, 11-19, 26-29, 32-38, 42-48 and 52-55 directed to an invention not patentably distinct from claims of commonly assigned 09/707,852. Specifically, the claims are not patentably distinct from claims 156-173 of 09/707,852 for the same reasons as set forth above with respect to the obviousness-type double patenting rejection of record.

19. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 09/707,852, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

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A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

*Response to Arguments*

20. Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection. Note new grounds of rejection have been made in view of the extensive amendments made to the claims and including subject matter that was not previously claimed.

*Conclusion*


21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephonic number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and all. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 571-272-1281. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
William H. Beisner  
Primary Examiner  
Art Unit: 1744

WHB